Amendments to the Claims

This listing of claims will replace all prior versions, and listings of claims in the application:

Listing of Claims:

1. (Withdrawn) A method for identifying candidate compounds for the modulation of signal transduction associated with a 7TM receptor, comprising:

(a) identifying a peptide region in the 7TM receptor ("*unique region*") by aligning the 2nd intracellular region of the 7TM receptor with the 2nd intracellular region of rhodopsin and determining the sequence of the 7TM receptor corresponding to positions 143-151 of rhodopsin;

(b) synthesizing at least one compound comprising a sequence selected from the group consisting of:

(b1) a sequence comprising of from a minimum of 5 continuous amino acids of said unique region to a maximum of all the continuous amino acids of said unique region;

(b2) a variant of the sequence of (b1) wherein up to 40% of the amino acids of the sequence of (b1) have been replaced with a naturally or non-naturally occurring amino acid or with a peptidomimetic organic moiety; and/or up to 40% of the amino acids have their

side chains chemically modified, and/or up to 20% of the amino acids have been deleted, provided that at least 50% of the amino acids of (b1) are maintained unaltered in the variant;

(b3) a sequence of (b1) or (b2) wherein one or more of the amino acids is replaced by the corresponding D-amino acid;

(b4) a sequence of any one of (b1) to (b3) wherein at least one peptidic backbone atom, or peptidic backbone bond has been altered to a modified peptidic backbone atom or a non-naturally occurring peptidic backbone bond, respectively;

(b5) a sequence of any one of (b1), (b2), (b3) or (b4) in a reverse order; and

(b6) a combination of two or more of the sequences of (b1), (b2), (b3), (b4) or (b5).

(c) testing each compound of (b) to determine the capacity thereof to modulate the signal transduction associated with the 7TM receptor.

2. (Withdrawn) A method according to Claim 1, further including after step (a) and prior to the step (b) the following steps:

(a.i) determining a continuous stretch of at least 5 amino acids of the unique region identified in Claim 1(a)

above, that is shorter than the length of the full unique region and modulates the signal transduction associated with the 7TM-receptor, by synthesizing a plurality of compounds each comprising one of a plurality of subsequences (optionally partially overlapping subsequences) of 5-9 aa which are present as a continuous sequence in the unique region; testing those compounds in a test assay for determining signal transduction associated with the 7TM receptor, and selecting those subsequences that modulates said 7TM-receptor-associated signal transduction; and

(a.ii) determining in the sequences of (a.i) essential and non-essential amino acids by: preparing a plurality of modified sequences wherein in each sequence a single and different amino acid of the native sequence has been replaced with a test amino acid to produce modified sequences; testing those modified sequences in a test assay for determining signal transduction associated with the 7TM receptor, identifying as essential amino acids those amino acids which when replaced, caused a statistically significant change in signal transduction; and

wherein said sequence of (b1) is a sequence determined by step(a.i) and wherein said sequence of (b2) is

the sequence, wherein at least one of the essential amino acids identified by the step of (a.ii) has been replaced by a conservatively substituted naturally or non-naturally occurring amino acid, or a conservative peptidomimetic organic moiety, and/or wherein at least one of the non-essential amino acids has been deleted, or substituted (conservatively or non-conservatively) by naturally or non-naturally occurring amino acids or a peptidomimetic organic moiety.

3. (Withdrawn) A method according to Claim 2 wherein the test amino acid is Alanine.

4. (Withdrawn) A method for obtaining a compound for the modulation of 7TM receptor- associated signal transduction the method comprising:

(a) identifying candidates for the modulation of signal transduction associated with the 7TM receptor according to the method of Claim 1;

(b) selecting from the candidates of (a) a compound that modulates signal transduction associated with the 7TM receptor in the test assay as compared to the modulation of the signal transduction associated with the 7TM receptor in the same test assay in the absence of the compound; and

(c) producing the compound of (b) thereby obtaining compounds for the signal transduction associated with the 7TM receptor.

5. (Withdrawn) A method according to Claim 4, wherein the test assay for determining 7TM receptor-associated signal transduction is selected from the group consisting of:

(a) an assay wherein the level of activation of at least one G-protein is determined;

(b) an assay wherein the level of at least one of the following 7TM receptor-associated signal transduction-dependent cellular property is determined: proliferation, apoptosis, differentiation, cellular-shape alteration, cellular elongation, gene expression, cell to cell contact, glucose uptake by cells, lipogenesis by adipose cells, and secretion of substances from cells; and

(c) an *in vivo* assay wherein the level of at least one of the following 7TM receptor-associated signal transduction physiological properties is determined: level of metabolites, hormones, or cytokines in circulation; size of induced or implanted tumor, number of metastases; weight alteration; appetite alteration, infection level; inflammation level; survival of tissue, mortality rates, glucose levels in blood.

6. (Withdrawn) A compound for the modulation of signal transduction associated with a 7TM receptor obtained by the method of Claim 4.

7. (Currently amended) A compound which has the property of modulation of signal transduction of a 7TM receptor consisting of: at least one moiety for transport across cellular membranes, in association with a peptide sequence of 4-55 amino acid residues selected from the group consisting of:

(a) a peptide sequence which is a continuous stretch of at least 5 amino acids present in the 7TM receptor in positions corresponding to the positions 143-151 of rhodopsin when the 2nd intracellular region of the 7TM receptor is aligned with the 2nd intracellular region of rhodopsin;

(b) a variant of the peptide sequence according to (a) wherein up to 40% of the amino acids of the native sequence have been replaced with a naturally or non-naturally occurring amino acid or with a peptidomimetic moiety; and/or up to 40% of the amino acids have their side chains chemically modified; and/or up to 20% of the amino acids have been deleted provided that at least 50% of the amino acids in the parent sequence of (a) are maintained unaltered ~~and~~ in the variant;

(c) a peptide sequence according to (a) or (b) wherein at least one of the amino acids is replaced with a corresponding D-amino acid;

(d) a peptide sequence according to any one of (a) – (c) wherein at least one of the peptidic backbones has been altered to a non-naturally occurring peptidic backbone;

(e) a peptide sequence being the sequence of any one of (a) – (d) in reverse order; and

(f) a combination of two or more of the peptide sequences of (a) to (e).

8. (Original) A compound according to Claim 7, wherein the moiety is a hydrophobic moiety.

9. (Withdrawn) A method for the modulation of signal transduction associated with a 7TM receptor in a subject comprising administering to the subject a therapeutically effective amount of a compound according to Claim 6.

10. (Withdrawn) A method for the treatment of a disease, wherein a therapeutically beneficial effect may be evident by the modulation of a signal transduction associated with a 7TM receptor, comprising:

administering to a subject in need of such treatment a therapeutically effective amount of a compound according to Claim 6 wherein the 7TM receptor from which the sequence in the

compound is obtained is determined, is the 7TM receptor associated with said signal transduction.

11. (Withdrawn) A method according to Claim 10, for the treatment of a disease selected from the group consisting of: hypertension, stroke, heart failure, neurodegenerative diseases (including Alzheimer's disease), renal disease, psychiatric disease, cancer, asthma, diabetes and immune disorders.

12. (Withdrawn) A method of detecting a ligand that binds to the unique region of a 7TM receptor, comprising:

(a) providing a compound according to Claim 6;

(b) incubating said compound with a sample, to be tested for the presence of said ligand, for a time sufficient for said ligand to bind to said compound; and

(c) detecting any said ligand-said compound binding pair that has been formed in step (b), wherein the presence of said ligand-said compound derivative binding pair establishes the existence of said ligand in said sample.

13. (Withdrawn) The method of Claim 12, further comprising the following steps after step (c):

(d) separating said ligand from said compound; and

(e) determining the structure of said ligand, thereby identifying said ligand.

14. (Withdrawn) A pharmaceutical composition comprising as an active ingredient at least one of the compounds of Claim 6.

Claims 15-17 (Cancelled).

18. (Withdrawn) A compound according to claim 6, comprising any of the sequences depicted in Fig. 1.

19. (Withdrawn) A pharmaceutical composition according to claim 14 comprising as an active ingredient a compound depicted in Fig. 1.

20. (Withdrawn) A method for the stimulation of angiogenesis comprising: contacting blood vessels with an effective amount of a compound comprising a sequence selected from the group consisting of:

(g) a sequence according to claim 7(a) which is a continuous stretch of at least 5 amino acids present in native EDG3 7TM receptor in residue positions 143 to 151;

(h) a variant of the sequence according to claim 7 (a) wherein up to 40% of the amino acids of the native sequence have been replaced with a naturally or non-naturally occurring amino acid or with a peptidomimetic moiety; and/or up to 40% of the amino acids have their

side chains chemically modified; and/or up to 20% of the amino acids have been deleted provided that at least 50% of the amino acids in the parent sequence of (a) are maintained unaltered and the variant, and provided that the variant has angiogenesis stimulating properties;

(i) a sequence according to claim 7 (a) or (b) wherein at least one of the amino acids is replaced with a corresponding D-amino acid;

(j) a sequence according to any one of claim 7 (a) - (c) wherein at least one of the peptidic backbones has been altered to a non-naturally occurring peptidic backbone;

(k) a sequence being the sequence of any one of claim 7 (a) - (d) in reverse order and;

(l) combination of two or more of the sequences of claim 7 (a) to (f).

Claim 21 (Cancelled).

22. (Withdrawn) A method according to claim 20, wherein the sequence of (a) is in residue positions 143-148 of the EDG3 7TM receptor.

23. (Withdrawn) A method according to claim 21, wherein the compound is R002L103 (SEQ ID NO:4).

24. (Withdrawn) A method according to claim 22, wherein the compound is R002L106 (SEQ ID NO:5).

25. (Withdrawn) A method for the treatment of a disease, wherein a therapeutically beneficial effect may be evident by stimulation of angiogenesis, comprising administering to an individual in need of such treatment an effective amount of a compound as defined in claim 20.

26. (Withdrawn) A method according to claim 25, wherein the disease is selected from the group consisting of coronary artery diseases, peripheral artery diseases, endothelial vascular diseases, arteriosclerosis, various processes of wound and tissue healing such as healing of bone tendon endothelial lining (such as in ulcers in the stomach or skin), for improving the success rate of cell transplantation techniques, in reconstructive surgery to help reestablish proper blood circulation to the reconstructed tissue.

27. (Withdrawn) A method for the modulation of signal transduction associated with a 7TM receptor in a subject, comprising administering to the subject a therapeutically effective amount of a compound according to Claim 7.

28. (Withdrawn) A method for the treatment of a disease, wherein a therapeutically beneficial effect may be

evident by the modulation of a signal transduction associated with a 7TM receptor, comprising:

administering to a subject in need of such treatment a therapeutically effective amount of a compound according to Claim 7, wherein the 7TM receptor, from which the sequence in the compound is determined, is the 7TM receptor associated with said signal transduction.

29. (Withdrawn) A method according to Claim 28, for the treatment of a disease selected from the group consisting of: hypertension, stroke, heart failure, neurodegenerative diseases (including Alzheimer's disease), renal disease, psychiatric disease, cancer, asthma, diabetes and immune disorders.

30. (Withdrawn) A method of detecting a ligand that binds to the unique region of a 7TM receptor, comprising:

(f) providing a compound according to Claim 7;

(g) incubating said compound with a sample, to be tested for the presence of said ligand, for a time sufficient for said ligand to bind to said compound; and

(h) detecting any binding pair of said ligand and said compound that has been formed in step (g), wherein the presence of said e binding pair establishes the existence of said ligand in said sample.

31. (Withdrawn) The method of Claim 30, further comprising the following steps after step (h):

(i) separating said ligand from said compound in said binding pair; and

(a) (j) determining the structure of said ligand, thereby identifying said ligand.

32. (Previously presented) A pharmaceutical composition comprising as an active ingredient at least one of the compounds of Claim 7.

33. (Previously presented) A pharmaceutical composition according to claim 32 comprising as an active ingredient a compound depicted in Fig. 1.

34. (Previously presented) A compound according to claim 7, comprising any of the sequences depicted in Fig. 1.